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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/546,201	04/10/2000	John M. Polo	930049.464/1463.002	3605

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/546,201	Applicant(s) POLO ET AL.	
	Examiner Shanon Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28-31 and 33-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28-31 and 33-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant amended claim 43 in paper no. 15. Claims 26, 28-31, and 33-44 are under consideration. It is most appreciated that Applicant submitted a clean copy of all pending claims with the response.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26, 28-31, and 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky et al. (US 6,015,686), i.e., "Dubensky", Polo et al. (Nature Biotechnology. 1998; 16: 517-518), i.e., "Polo", and Cella et al. (J. Exp. Med. 1999; 189 (5): 821-829), i.e., "Cella" for reasons of record.

Applicant asserts that a prima facie case of obviousness has not been established without some objective reasoning for combining the teachings in the references. Applicant cites case law supporting the assertion that individual elements cannot be picked and chosen individually in references and that a prima facie case of obviousness has only been established if the motivation for combining the teachings is found in the references themselves. Applicant also argues, and cites supporting case law, that the disclosed invention may not be used as a template for impermissible hindsight. Applicant states that a prima facie obvious case has not been established because there is no teaching or suggestion for every element in the instant claims, and therefore, no motivation to combine the elements. Specifically, Applicant argues that the

Dubensky reference is silent with respect to the formation of a double-stranded RNA that induces interferon production. The reference also does not teach an RNA polymerase II promoter to express a pathogenic agent. Applicant points out that the instant RNA Pol II promoter is a DNA-dependent RNA promoter rather than an RNA-dependent RNA promoter, as taught in Dubensky. Applicant concludes that the teachings of Cella and Polo fail to remedy the deficiencies of Dubensky and do not teach constructs having two promoters in which one encodes an antigen and the other is an RNA Pol II promoter.

Applicant's arguments and a review of the cited case law and the references have been considered, but are found unpersuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Applicant's attention is directed to the second paragraph of MPEP § 2143, which states that the motivation to make the claimed combination and the reasonable expectation of success cannot be found in applicant's disclosure. Therefore, a different motivation to combine taught by the prior art, other than that taught by applicant is proper. The test of obviousness is not an express suggestion of the claimed invention in any or all references but what references taken together would suggest to those of ordinary skill in the

art presumed to be familiar with them. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art (emphasis added). See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a prima facie obvious case has been established because the three criteria of meeting the burden to establish obviousness have been met. First, the prior art cited against the instant application teaches all of the limitations in the claims. Second, a motivation to combine the references is found in the prior art. Third, a reasonable expectation of success has been established for producing the claimed invention when the prior art references are combined.

In the instant case, the cited prior art teaches all of the limitations in the claims. Dubensky (6,015,686) teaches a eukaryotic layered vector initiation cassette that expresses a heterologous sequence from RSV, HPV, HBV, HCV, EBV, HIV, HSV, FeLV, FIV, Hantavirus, HTLV I, HTLV II, and CMV, under the control of an RNA polymerase II promoters see claim 9 and column 4, lines 36-46, and column 114, lines 30-37. Dubensky also teaches that the vector system expression of bacterial, fungal, and parasitic antigens, see column 28, lines 4-19, and/or be anti-cancer related, see column 27, line 60 to column 28, line 2. These teachings of Dubensky teach the second segment of instant claim 26 in which an RNA Pol II promoter encodes a

pathogenic agent, as well as claims 28, 29, 30, 31, and 43. The reference also teaches that the vector can utilize any of the promoters listed in claim 33, see column 4, lines 8-12 and that retrovirus, herpesvirus, poxvirus, alphavirus, adenovirus, and polyomavirus are used as vectors in the vector initiation system as gene delivery vehicles, see column 32, lines 26-68 and column 80, line 17 to column 81, line 31, which are the elements of instant claims 34-42. The reference further teaches that the system is expressed in a cell line, see claims 12-15 and 20. Therefore, Dubensky teaches all of the individual elements in the instant claims, except for expressing a dsRNA in the vector system to induce the production of interferon, which is the first part of claim 26.

Although Dubensky does not expressly teach this limitation, the reference does teach that more than one heterologous sequence is expressed in the vector system, see column 28, lines 4-19, and is not limited to antigens from pathogens, but also includes other forms of nucleotides, such as those encoding non-coding sequences, see claim 10. This embodiment of Dubensky encompasses any non-coding nucleotide sequence, including the instant dsRNA. However, since this element is not expressly taught in the reference, the second aspect of making a prima facie obvious case must be met, that is, a motivation to specifically express a dsRNA to induce the production of interferon. This second burden is met by combining the teachings of Cella and Polo, which demonstrate the knowledge generally available to one of ordinary skill in the art (emphasis added), see *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Cella et al. (J Exp. Med. March 1, 1999; 189 (5): 821-829) teach dendritic cells activated by dsRNA increases antigen presentation and activate naïve T cells and stimulate T

helper responses. Polo et al. (Nature Biotechnology. June 1998; 16 (6): 517-518) teach that alphavirus vector RNA molecules replicate through dsRNA intermediates that are able to induce production of interferons, see the first and second columns on page 518.

One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate dsRNA into the expression cassette taught by Dubensky et al. to increase viral antigen presentation taught by Cella et al. and induce interferon production, taught by Polo et al. One would be further motivated to induce expression of the dsRNA with a different promoter from the RNA polymerase II promoter that expresses the antigen because one would want to be able to separately control the amount of expression of the antigen and the dsRNA. Therefore, motivation to combine the teachings in the references has been established based on general knowledge and specific teachings in the art.

The last criterion for meeting the burden for establishing a prima facie obvious case has also been established. One of ordinary skill in the art would have had a reasonable expectation in producing the claimed invention because Dubensky et al. teach that the eukaryotic layered gene delivery initiation system is used to stimulate the immune response against different pathogens by expressing more than one antigen with different promoters, which also express non-coding nucleic acid sequences and Cella and Polo teach expressing non-coding dsRNAs to stimulate the immune system against different pathogens.. Therefore, the three requirements for a prima facie obvious case have been satisfied and it is maintained that the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

It is noted in Applicant's response that Dubensky's RNA Pol II promoter and the instant promoter are different in that one is DNA-dependent and the other is RNA-dependent. This limitation is not in the instant claims. Also, even if the limitation were present, it would be obvious to the skilled artisan at the time the invention was made to select the RNA Pol II promoter that is most appropriate for a given application. However, this observation is moot since the discrepancy between Applicant's promoter and Dubensky's is not recited in the claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
June 21, 2002

James C. Housel 7/1/02

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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